DOCKET NO: PHRM0018-100/00188.US1 **PATENT**
Serial No.: 09/899,495 **Filing Date: July 5, 2001**

REMARKS

Claims 1-148 were pending in the application. Claims 1-104 and 110-148, withdrawn from consideration as directed to non-elected inventions, and claims 105 and 106 have been cancelled without prejudice. Claims 107-109 have been amended. New claims 149-152 have been added.

Claims 107-109 have been amended. Claim 107 was amended to make the claim independent and to further clarify the claim language. Claims 108 and 109 were amended to update the dependencies.

New claim 149 recites a polypeptide having 95% homology to SEQ ID NO:116, wherein the polypeptide has no more than 471 amino acid residues. New claim 150 recites that the polypeptide encodes a human $5HT_3$ serotonin receptor, wherein the polypeptide comprises an amino acid sequence with at least 95% sequence homology to SEQ ID NO:116 and wherein the polypeptide comprises the sequence Met-Leu-Ala. New claim 151 recites that the polypeptide of claim 150 has the Met-Leu-Ala sequence at the amino terminus of the polypeptide. New claim 152 recites that the polypeptide comprises at least one conservative substitution.

Support for the claim amendments and the new claims can be found throughout the specification and sequence listing as filed including, *inter alia*, in paragraph [00119] which recites that the "invention also embraces polypeptides that have at least 99%, at least 95%, at least 90%, at least 85%, at least 80%, at least 75%, at least 70%, at least 65%, at least 60%, at least 55% or at least 50% identity and/or homology ..." Support for new claims 149-152 can be found, for example, in the Sequence Listing which recites the length of SEQ ID NO:116 as 471 amino acid residues and that the polypeptide comprises a Met-Leu-Ala sequence. Support for new claim 152 can be found, for example, in Table 4 of the present application which recites conservative substitutions for a given amino acid residue.

No new matter has been added.

Upon entry of this amendment, claims 107-109 and 149-152 will be pending.

Objections

Claim 105 stands objected for the recitation of "SEQ ID NO:116 SEQ ID NO:116". Claims 106-109 are objected to since they depend from claim 105. Claims 105 and 106 have been cancelled without prejudice. Claims 107-109, as amended, no longer depend from claim 105. The objection to claims 105-109 is, therefore, moot.

Claims 105-109 were further objected to "since the syntax could be improved". Claims 105 and 106 have been cancelled without prejudice. Although Applicants respectfully assert that the claims would be readily understood by the art-skilled, Applicants have amended claim 107 to further clarify the claimed invention. Applicants do not expect the scope of the claims to be altered as a result of the amendment of claim 107.

In view of the foregoing, Applicants respectfully request that the objections to the claims be withdrawn.

Rejections under 35 U.S.C. § 112, first paragraph

Claims 105-109 stand rejected under 35 U.S.C. § 112, first paragraph, because, according to the Office, the specification does not "reasonably provide enablement for polypeptides which are 'at least 95% identical' to SEQ ID NO:116 and 'encode a serotonin receptor." (Office Action, page 4). The Office further asserts that even though "Applicants have demonstrated that the receptor of the present invention belongs to the 5-HT3 subfamily of human serotonin receptors ... [the scope of claim 105] includes serotonin receptors "from species other than human." Applicants respectfully disagree.

Preliminarily, Applicants note that claims 105 and 106 have been cancelled without prejudice. Claims 107-109 do not recite 95% homology to SEQ ID NO:116. The scope of the pending claims is such that the skilled artisan could readily practice the claimed invention without any undue experimentation.

The application as filed sets forth several examples of assays that could be employed by the art-skilled to determine whether a particular polypeptide falls within the scope of the pending claims. For example, Applicants provide methods for assaying for

ion channel polypeptide-interacting proteins (Example 7), methods for analyzing protein-protein interactions involving ion channel polypeptides (Example 8), and assays to identify modulators of ion channel activity (Example 9). Further, at the time of filing of the present application, the art-skilled would readily be able to differentiate human $5HT_3$ receptors from other receptors based on, *inter alia*, known binding characteristics, with no undue burden. As discussed in the specification, "5-HT3 receptors are structurally distinct and belong to the neurotransmitter-gated ion channel superfamily." (*see* [00006]).

One of skill in the art could also practice the invention of new claims 149-152 which recite structural and functional limitations in addition to the recited level of homology.

Claims 105-107 and 109 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to reasonably convey to the art skilled that applicant had possession of the invention at the time of filing. The Office alleges that although "Applicants have demonstrated that the receptor of the present invention belongs to the 5-HT_3 subfamily of receptors ... the limitation recited in claim 105 includes, in scope, any serotonin receptor from any subfamily, as well as from species other than human." Further, the Office notes that "the scope of the claims includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted ..." Applicants respectfully disagree because the art-skilled would readily understand that Applicants possessed the claimed invention at the time of filing.

As discussed above, claims 105 and 106 have been cancelled without prejudice. Claims 107-109 have been amended. Claim 107 has been amended to recite that the polypeptide encodes a ***human 5HT$_3$*** serotonin receptor, therefore excluding non-human receptors and serotonin receptors that are in different subclasses of serotonin receptor (*i.e.* $5HT_1$, $5HT_2$, and $5HT_4$).

Applicants were also clearly in possession of new claims 149-152. As discussed above, new claims 149-152 recite structural and functional limitations in addition to the stated levels of homology, limiting the scope of the claimed genus. Applicants note that the general knowledge of the art-skilled supplements the written description set forth in

the originally filed application. As discussed above, in the originally filed application Applicants noted that "5-HT3 receptors are structurally distinct [from other 5-HT receptors] and belong to the neurotransmitter-gated ion channel superfamily." Accordingly, the art skilled would readily appreciate the common attributes and characteristics of ***human 5HT$_3$*** receptors and would acknowledge that the disclosure of a single amino acid sequence, SEQ ID NO:116, was sufficient to describe the genus.

Applicants respectfully request the withdrawal of the rejections under 35 U.S.C. 112, first paragraph.

Rejections under 35 U.S.C. 102(e)

Claims 105 and 106 stand rejected under 35 U.S.C. 102(e) as allegedly anticipated by Wood *et al.* (cite). Applicants have cancelled claims 105 and 106 without prejudice, rendering the rejection moot.

New claims 149-152 have been added. Wood fails to anticipate claim 149 as Wood does not disclose a polypeptide comprising no more than 471 amino acid residues. Wood fails to anticipate claims 150 or 151 as Wood does not disclose a polypeptide comprising the sequence Met-Leu-Ala.

Applicants respectfully request the withdrawal of the rejections under 35 U.S.C. 102(e).

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Conclusion

Applicants believe the claims are in condition for allowance. An early Notice of Allowance is therefore earnestly solicited. Applicants invite the Examiner to contact the undersigned at (215) 665-6904 to clarify any unresolved issues raised by this response.

Respectfully submitted,

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